

CLAIMS

1. Automatic device (100) for producing a plurality of reaction samples from several constituents for implementing chemical or biological reactions in liquid medium, in particular the dosing of at least one particular constituent or analyte in a biological specimen, characterized in that it comprises:
- a first supply plate (110), in particular a removable plate of the microplate type, comprising N receptacles each intended to contain a constituent,
  - a second supply plate (120), in particular a removable plate of the microplate type, comprising M receptacles each intended to contain a constituent,
  - a removable plate for samples (130), comprising a plurality of cavities arranged in the form of an array (131) comprising at least N rows and at least M columns, each cavity exhibiting a volume of the order of a few tens of nanoliters, and being intended to contain a mixture of constituents originating from the first and second supply plates (110, 120),
  - a piezoelectric micropipette (141; 142) able to sample a determined amount of constituent and to deliver drops of volume of the order of a nanoliter,
  - means for displacing the piezoelectric micropipette along at least two perpendicular axes Y, Z so that it can sample from each filled receptacle of the first and second supply plates (110, 120), the determined amount of a constituent, and
  - means of relative displacement (101) of the piezoelectric micropipette (141; 142) and of the sample plate (130), which are associated with means for triggering discharge of the micropipette (141; 142) in such a way that the latter delivers at least one drop of constituent into each cavity of the sample plate (130).
2. Device according to Claim 1, characterized in that the relative displacement of the piezoelectric

micropipette (141; 142) and of the sample plate (130) is continuous and the discharge triggering means are able to trigger discharges of the micropipette at regular time intervals as a function of the constant speed of relative displacement of said micropipette (141; 142) and of the sample plate (130), independently of the presence or otherwise of a cavity of the sample plate (130) in line with said micropipette.

3. Device according to either of Claims 1 and 2, characterized in that the means of relative displacement (110) are means for advancing the sample plate (130) along an axis X parallel to the rows of the arrays (131) of cavities, and/or along an axis Y parallel to the columns of the arrays (131) of cavities, the piezoelectric micropipette (141; 142) remaining stationary above the sample plate (130) during the filling of said cavities.

4. Device according to either of Claims 1 and 2, characterized in that the means of relative displacement are means for advancing the micropipette along axes X and/or Y respectively parallel to the rows and to the columns of the arrays of cavities of the sample plate which remains stationary beneath said piezoelectric micropipette, during the filling of said cavities.

5. Device according to either of Claims 3 and 4, characterized in that the advancing means comprise a stepper or DC motor, and the discharge triggering means comprise a counter of the steps of the motor able to send a discharge triggering signal every  $N_1$  steps.

6. Device according to one of the preceding claims, characterized in that the piezoelectric micropipette (141; 142) is able to count the number of drops which it delivers and to stop discharging after a determined number of drops delivered.

7. Device according to one of the preceding claims, characterized in that it comprises a refrigerating tray supporting the sample plate (130).

8. Device according to one of the preceding claims, characterized in that there is provided at least one optical system (161; 162) such as the emission/reception of a laser carpet, in line with the sample plate (130), able to count the number of drops delivered with each discharge of the piezoelectric micropipette (141; 142), and to transmit this number to a coordination device so that an order for a second pass in line with a cavity or several cavities is sent to the micropipette when a discrepancy is noted between the counted number of drops discharged and the designated theoretical number of drops.

9. Device according to one of the preceding claims, characterized in that it comprises another piezoelectric micropipette (142) identical to the first (141), the two micropipettes (141; 142) operating alternately.

10. Device according to one of the preceding claims, characterized in that it comprises an automatic washing station (170) associated with each piezoelectric micropipette (141; 142) ensuring the decontamination of the latter.

11. Device according to Claim 10, characterized in that each washing station (170) comprises means for filling the piezoelectric micropipette (141; 142) with a water-immiscible carrier liquid and optical means (171) for verifying the proper filling of said micropipette (141; 142).

12. Device according to one of the preceding claims, characterized in that each piezoelectric micropipette (141; 142) comprises two conducting parts separated by a nonconducting material, which are linked at the upper part to an electrical system, so that when the orifice of the piezoelectric micropipette comes into contact with a constituent of a receptacle of the first or of the second supply plate, it brings about closure of the electrical circuit formed by the two electrically linked conducting parts of said

micropipette, which commands the stoppage of the vertical displacement of the micropipette.

IMD 13. Device according to one of the preceding claims, characterized in that there is provided an  
5 automatic means (190) for fitting a seal on the sample plate (130).

IMD 14. Device according to one of the preceding claims, characterized in that there is provided an  
10 automatic means with suckers (180) for removing and for fitting covers on the first and second supply plates (110, 120) as well as on the filled sample plate (130).

IMD 15. Device according to one of the preceding claims, characterized in that the first and second supply plates (110, 120) are disposed along the X axis  
15 on either side of the supply plate (130), said plates (110, 120, 130) together being carried by a movable bench (110) along said X axis.

IMD 16. Device according to any one of the preceding claims, characterized in that the arrays (131) of  
20 cavities of the sample plate (130) is a square arrays with N equal to M.

IMD 17. Device according to Claim 16, characterized in that said arrays (131) exhibits a width of around 5 cm, and in that it comprises 100 columns and 100 rows with  
25 cavities of width ( $d_1$ ) equal to around 400  $\mu\text{m}$  and of depth equal to around 400-500  $\mu\text{m}$ , two successive cavities in one row being spaced apart by a distance ( $d_2$ ) equal to around 150  $\mu\text{m}$ .

IMD 18. Device according to any one of the preceding claims, characterized in that it comprises other  
30 vessels (151, 152) of different constituents disposed in proximity to the sample plate (130).